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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: PROTEIN COMPLEXES OF THE TIP60 TRANSCRIPTIONAL ACTIVATOR PROTEIN

(57) Abstract: The present invention relates to the TIP60-transcriptional activator protein complex, which is a part of the beta-amy-
loid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the com-
ponent proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of these complexes
and the interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

WO 2004/009619 A3

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 03/07848

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N15/62 C12N9/10 C07K14/47 C07K16/18
C12Q1/68 A61K38/00 A01K67/027 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IKURA TSUYOSHI ET AL: "Involvement of the TIP60 histone acetylase complex in DNA repair and apoptosis" CELL, vol. 102, no. 4, 18 August 2000 (2000-08-18), pages 463-473, XP002267408 ISSN: 0092-8674 cited in the application the whole document --- -/--	1-10,12, 17-21, 25-32, 35-45

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

20 January 2004

Date of mailing of the international search report

01/03/2004

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INTERNATIONAL SEARCH REPORT

International Application No.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RIGAUT G ET AL: "A generic protein purification method for protein complex characterization and proteome exploration" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 17, no. 10, October 1999 (1999-10), pages 1030-1032, XP002179540 ISSN: 1087-0156 cited in the application the whole document	9-11
X	WO 02 22660 A (HYSEQ INC ;WEHRMAN TOM (US); YANG YONGHONG (US); ZHANG JIE (US); Z) 21 March 2002 (2002-03-21) see SEQ ID NO: 19 and 463 page 1 -page 6; claims 1-28	13-16, 23,24
X	WO 01 57190 A (CAO YICHENG ;CHEN RUI HONG (US); GOODRICH RYLE (US); HYSEQ INC (US) 9 August 2001 (2001-08-09) see SEQ ID NO: 1257 page 1 -page 6; claims 1-28	13-16, 23,24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/07848

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 42-44 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 12 (partially), 22, 33, 34
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 12 (partially), 22, 33,34

Claims 1-11, 13-21, 23-32, and 35-45 relate to 'derivatives', 'fragments' and 'homologs' defined by reference to a desirable characteristic or property, namely having the activity of the protein from which they were derived. In particular, claim 13 is directed to proteins named 'C20orf20' and 'KIAA1093 (Fragment)', which are of unknown function, while the claim extends to functional fragments and derivatives. The application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for any such variants. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved.

Said claims also relate to 'variants' of a protein, encoded by a nucleic acid which hybridises under low stringency conditions to the nucleic acid which encodes the protein of which they are variants. The number of 'variants' within the scope of such a claim is so large, that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises.

Claim 8 relates to a complex having a biochemical activity, namely transcriptional or apoptotic activity, where the only complex with such activity disclosed in the sense of Art.5 PCT or supported in the sense of Art.6 PCT in the application is the protein complex containing the complex members with SEQ ID NO: 1-18.

Claim 17 relates to an antibody or a fragment thereof which binds to a complex, but not to any of its uncomplexed components. The application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for any such antibodies. Independently, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved.

The above objections render a meaningful search of the entire scope of the claims impossible. In view thereof, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely a protein complex containing the complex members with SEQ ID NO: 1-18, constructs encoding them and host cells comprising the construct, antibodies directed to said complex, kit comprising the complex or the antibody or the construct or the host, array comprising said complex or antibody, composition comprising said complex, method for screening for binding molecules and/or modulators of said complex, and method of diagnosis on the basis of the presence of said complex.

Claim 12 relates to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

proteins that have been identified by using TIP60 polypeptide (SEQ ID NO: 17) as bait, namely the polypeptides with SEQ ID NO: 1-16 and 18.

Claims 33 and 34 relate to compounds identified by a method, where no such compounds are disclosed in the application in the sense of Art.5 PCT or supported in the sense of Art.6 PCT. Claim 22 is directed to the use of the complex for modulating a substrate, where no such substrate is disclosed or supported. A meaningful search of these four claims was completely impossible. Consequently, the present search report does not extend to these four claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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